defining the position of expected peaks using known possible peak areas from the biological sample;

shifting the corrected data set to more closely align the putative peaks to the expected peaks;

calculating a probability that the putative peaks in the shifted data set are actual peaks;

determining a confidence of the probability; and

if the confidence exceeds a threshold value, using the putative peaks to identify a component in the sample.

REMARKS

Any fees that may be due in connection with this application throughout its pendency may be charged to Deposit Account No. 50-1213.

Claims 1-45 are presently pending in this application. Claims 1, 38, 40 and 45 are amended herein to more distinctly claim the subject matter claimed by the applicant.

In compliance with our duty of disclosure, the Examiner's attention is directed to co-pending U.S. application Serial No. 09/285,481, filed April 2, 1999, by Köster *et al.* It is noted that if any rejections for obviousness-type double patenting are initiated, then any Action with such rejection cannot be made final.

Claims 1, 38, 40 and 41 are amended herein to recite "comprising data of the components in the biological sample" to more particularly point out and distinctly claim the subject matter claimed by the applicant, basis for which is found in the specification (for example, see page 22, lines 6-15 and page 24, lines 15-18). Claims 40 and 45 are amended to correct minor typographical errors. Claim 45 is also amended to include determining a confidence and identifying a component in the sample using putative peaks when the [illegible] throughout the specification (for example, see page [illegible] lines [illegible] 26 and page [illegible] line 1 through page 20, line 22).

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No new matter is added nor are any amendments made to change the scope of the claims. Included as an attachment is a marked-up version of the amended claims, as per 37 CFR §1.121. A Supplemental Information Disclosure Statement also accompanies this amendment. The amendments should place the claims and the application into condition for allowance.

REJECTION OF CLAIMS 1-45 UNDER 35 U.S.C. §112, FIRST PARAGRAPH - ENABLEMENT

Claims 1-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make or use the claimed subject matter. The Examiner alleges that the steps of "correcting the baseline," "removing the residual baseline from the intermediate data set," and "locating a probable peak" are not enabled. In particular, the Examiner alleges that the specification fails to:

1. recite or contain adequate support for "components attributable to the test system" or "components attributable to the sample preparation characteristics" (page 8, lines 13-21) and alleges that "correcting the baseline" requires this information;
2. disclose the exact quartic polynomial applied in "removing the residual baseline" that allegedly requires a quartic polynomial, and alleges that without the quartic polynomial applied one of skill in the art would not understand how to perform the step; and
3. provide a set of possible compositions or expected peaks to which to match the putative peaks obtained for use in the step "locating a probable peak," and alleges that one of skill in the art would be unable to match the putative peaks with the expected peaks.

The Examiner alleges that it would require undue experimentation to make and

This rejection is respectfully traversed.

RELEVANT LAW

The test of enablement is whether one skilled in the art can make and use what is claimed based upon the disclosure in the application and information known to those of skill in the art without undue experimentation. *United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). A certain amount of experimentation is permissible as long as it is not undue. To satisfy the enablement requirement of 35 U.S.C § 112, first paragraph, the specification must teach one of skill in the art to make and use the invention without undue experimentation. *Atlas Powder Co. v. E.I. DuPont de Nemours*, 750 F.2d 1569, 224 USPQ 409 (1984). This requirement can be satisfied by providing sufficient disclosure, either through illustrative examples or terminology, to teach one of skill in the art how to make and how to use the claimed subject matter without undue experimentation. This clause does not require "a specific example of everything *within the scope* of a broad claim." *In re Anderson*, 176 USPQ 331, at 333 (CCPA 1973), emphasis in original. Rather, the requirements of § 112, first paragraph "can be fulfilled by the use of illustrative examples **or** by broad terminology." *In re Marzocchi et al.*, 469 USPQ 367 (CCPA 1971)(emphasis added).

The "invention" referred to in the enablement requirement of section 112 is the claimed subject matter. *Lindemann Maschinen-fabrik v. American Hoist and Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984) ("The question is whether the disclosure is sufficient to enable those skilled in the art to practice the claimed invention"); *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 956, 220 USPQ 592, 596 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835, 225 USPQ 232 (1984).

It is incumbent upon the examiner to first establish a *prima facie* case of non-enablement. *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369-70

> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt does exist, a rejection for failure to teach how to make and/or use will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the teaching contained in the specification is truly enabling. . . it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

Id. (emphasis in original); *See also Fiers v. Revel*, 984 F.2d 1164, 1171-72, 25 USPQ2d 1601, 1607 (Fed. Cir. 1993);, *Gould v. Mossinghoff*, 229 USPQ 1, 13 (D.D.C. 1985), *aff'd in part, vacated in part, and remanded sub nom. Gould v. Quigg*, 822 F.2d 1074, 3 USPQ2d 1302 ("there is no requirement in 35 U.S.C. § 112 or anywhere else in patent law that a specification convince persons skilled in the art that the assertions in the specification are correct"). A patent application need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent , Inc.*, 3 USPQ2d 1737 (Fed. Cir. 1987).

The inquiry with respect to scope of enablement under 35 U.S.C. § 112, first paragraph, is whether it would require undue experimentation to make and use the subject matter as claimed. A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art [illegible] factors [illegible] *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int [illegible] 1986); see also *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

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PTO GUIDELINES

The PTO has promulgated guidelines, which incorporate the above-noted law, for examining chemical/biotechnical applications with respect to 35 U.S.C. §112, first paragraph, enablement. As set forth in the guidelines, the standard for determining whether the specification meets the enablement requirement is whether it enables any person skilled in the art to make and use the claimed invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400 (Fed. Cir. 1988). In determining whether any experimentation is "undue," consideration must be given to the above-noted factors.

As indicated in the published PTO guidelines, it is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The analysis must consider all the evidence related to each of the factors, and any conclusion of non-enablement must be based on the evidence as a whole. *Id.* 8 USPQ2d at 1404 & 1407.

The starting point in an evaluation of whether the enablement requirement is satisfied is an analysis of each claim to determine its scope. The focus of the inquiry is whether everything within the scope of the claim is enabled. As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. *In re Moore*, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971). Once the scope of the claims is addressed, a determination must be made as to whether one skilled in the art is enabled to make and use the entire scope of the claimed invention without undue experimentation.

ANALYSIS

The Office Action fails to establish a *prima facie* case of lack of enablement pursuant to [illegible] first paragraph.

The examiner alleges that three steps in claims [illegible] and all claims dependent therefrom are not enabled. It is alleged in the Office Action

that the steps of "correcting the baseline," "removing the residual baseline from the intermediate data set," and "locating a probable peak" are not enabled in the specification. This rejections is respectfully traversed.

As discussed below, the claims are commensurate in scope with the disclosure, which exemplifies particular embodiments within the scope of the claims and teaches how one of skill in the art can practice other embodiments within the scope of the claims. In particular, there is a substantial amount of guidance presented in the specification, the level of skill in the art is high, there are several working examples, and the type of experimentation, in view of the disclosure in the application, is routine. Thus, it would not require undue experimentation for one of skill in the art to make and use the claimed subject matter.

Evaluation of the above Factors

1. The scope of the claims

Claim 1 is directed to a method for identifying a biological sample, which includes generating a data set including data of the components in the biological sample; denoising the data set to generate denoised data; correcting the baseline from the denoised data to generate an intermediate data set; defining putative peaks for the biological sample; using the putative peaks to remove residual baseline effects, generating a residual baseline; removing the residual baseline from the intermediate data set to generate a corrected data set; locating a probable peak in the corrected data set; and identifying, using the located probable peak, the biological sample. Claims 2-37 depend from claim 1 and are directed to various embodiments thereof.

Claim 38 is directed to a system for identifying a biological sample that includes an instrument receiving the biological sample and generating a data set including data of the components in the biological sample; a computer

[illegible]

set, where the computer denoises the data set to generate denoised data; corrects the baseline from the denoised data to generate an intermediate data

set; defines putative peaks for the biological sample; uses the putative peaks to remove residual baseline effects, generating a residual baseline; removes the residual baseline from the intermediate data set to generate a corrected data set; locates a probable peak in the corrected data set; and identifies the biological sample using the located probable peak. Claim 39 depends from claim 38 and is directed to the embodiment where the computer is integral to the instrument.

Claim 40 is directed to a machine readable program operating on a computing device, where the computing device is configured to receive a data set including data of the components in a biological sample, where the program denoises the data set to generate denoised data; corrects the baseline from the denoised data to generate an intermediate data set; defines putative peaks for the biological sample; removes residual baseline effects using the putative peaks to generate a residual baseline; removes the residual baseline from the intermediate data set to generate a corrected data set; locates a probable peak in the corrected data set; and identifies, using the located probable peak, the biological sample.

Claim 41 is directed to a system for identifying a component of a DNA sample, including a mass spectrometer receiving the DNA sample and generating a data set including data of the components in the DNA sample; a computing device configured to receive the data set, the computing device implementing the method including denoising the data set to generate denoised data; correcting the baseline from the denoised data to generate a corrected data set having putative peaks; using the putative peaks to remove residual baseline effects; locating a probable peak in the corrected data set; and identifying, using the located probable peak, a component in the composition of the DNA sample. Claims 42-44 depend from claim 41 and are directed to various embodiments thereof

biological sample, including an instrument receiving the biological sample and generating a data set including data of the components in the biological sample;

a computing device receiving the data set and performing the steps of generating corrected data by processing the data set to remove noise due to system and chemical reaction characteristics, the corrected data set having putative peak areas; using the putative peaks to remove residual baseline effects; defining the position of expected peaks using known possible peak areas from the biological sample; shifting the corrected data set to more closely align the putative peaks to the expected peaks; calculating a probability that the putative peaks in the shifted data set are actual peaks; determining a confidence of the probability; and if the confidence exceeds a threshold value, using the putative peaks to identify a component in the sample.

2. Level of skill in the art

In this instance, the level of skill in the art is high. This is evidenced by the art in this area, which is authored primarily by those with Ph.D. and M.D. degrees and is intended for an audience of similarly highly skilled individuals, primarily in the fields of biochemical, chemical, pharmaceutical, or medical arts. The numerous articles and patents made of record in this application, authored and reviewed by those known in the art, address a highly skilled audience, and further evidence the high level of skill in this art.

3. State of the Art

At the time of filing of the instant application, a broad body of knowledge had amassed in the areas of pharmaceutical sciences, medicine, chemistry and biochemistry directed to the use of analytical methods and devices for identifying a sample or the components in a compound. Many of these articles and patents have been made of record in this application.

These references to numerous published protocols and instruments for identifying a sample or the composition of a compound demonstrate the large state of the art at the relevant time.

4. The amount of direction and guidance presented, teachings in the specification and presence of working examples

The specification provides a detailed amount of direction and guidance for the methods and systems for identifying a biological sample as instantly claimed, as discussed in detail below.

Correcting the baseline

The specification teaches on page 8, lines 16-24 that the

> denoised data then has a baseline correction applied in block 50. A baseline correction is generally necessary as data coming from the test instrument, in particular a mass spectrometer instrument, has data arranged in a generally exponentially decaying manner. This generally exponential decaying arrangement is not due to the composition of the biological sample, but is a result of the physical properties and characteristics of the test instrument, and other chemicals involved in DNA sample preparation. Accordingly, baseline correction substantially corrects the data to remove a component of the data attributable to the test system and sample preparation characteristics.

The Examiner contends that the components attributable to the test system and the components attributable to the sample preparation characteristics are absent from the specification and thus "correcting the baseline" is not enabled. The applicant respectfully submits that the Examiner is mistaken. The specification teaches that the baseline correction corrects the data <u>**to**</u> <u>**remove**</u> a component attributable to the test system and sample preparation characteristics, not <u>**BY**</u> <u>**removing**</u> a component attributable to the test system or attributable to the sample preparation characteristics.

Further, the specification teaches methods to generate a baseline correction, and provides working examples. For instance, Figure 15 discloses an exemplary method used to generate a baseline correction that includes the steps of performing a wavelet transformation on the peak free signal, deleting all

4, line 24 through page 15, line 2 that

> a process of using the peak-free signal 155 to generate a baseline 170 as shown in FIG. 16. As shown in block 162, a wavelet transformation is performed on the peak-free signal 155. All the stages from the wavelet transformation are eliminated in block 164 except for the n low stage. The n low stage will generally indicate the lowest frequency component of the peak-free signal 155 and therefore will generally indicate the system exponential characteristics. Block 166 shows that a signal is reconstructed from the n low coefficients and the baseline signal 170 is generated in block 168.

Thus, the method used to correct the baseline does not depend on knowing a component attributable to the test system or a component attributable to the sample preparation characteristics, as alleged by the Examiner. Instead, a wavelet transformation corrects the baseline. The instant specification teaches that, in addition to wavelet transformation, conventional analysis techniques such as Fourier analysis techniques for signal processing and numerical analysis can be used (page 8, lines 4-6).

Therefore, one of skill in the art, by virtue of applicant's teachings in the specification, the working examples provided in the specification and known procedures in the art, would be able to use the claimed baseline correction method that includes signal processing and numerical analysis techniques, such as wavelet transformation to remove a component from the data attributable to the test system and due to sample preparation characteristics.

<u>Removing the residual baseline</u>

The Examiner contends that in order to remove the residual baseline a residual baseline must be generated, and contends that the specification indicates that a quartic polynomial is used to generate the residual baseline. The Examiner alleges that the specification does not disclose the quartic polynomial applied to the data to generate such a residual baseline, and that without this formula for the quartic polynomial applied, one of skill in the art [illegible] in order to remove the residual baseline.

It is respectfully submitted that the quartic polynomial is a well-known equation, of the form

$$ax^4 + bx^3 + cx^2 + dx + e = 0$$

which is used by those of skill in the art for curve fitting and approximations for complicated linear systems (see Catherall, U.S. Patent 4,031,370; 1977). The coefficients are varied to provide the best fit to the data, and a method for determining the polynomial coefficients is described in detail by Catherall *et al.* (U.S. Patent 3,789,203; 1974). The specification teaches that techniques other than using a quartic polynomial can be used to smooth or fit the residual baseline. For example, the specification teaches on page 18, lines 16-23 that

> peaks are removed and remaining minima 247 located as shown in FIG. 23 with the minima 247 connected to create signal 245. A quartic polynomial is applied to signal 245 to generate a residual baseline 250 as shown in FIG. 24. The residual baseline 250 is subtracted from the signal 225 to generate the final signal 255 as indicated in FIG. 25. Although the residual baseline is the result of a quartic fit to signal 245, it will be appreciated that other techniques can be used to smooth or fit the residual baseline.

The specification thus teaches that a quartic polynomial or <u>other technique</u> known to one skilled in the art <u>to smooth or fit the residual baseline</u> is used to generate a residual baseline. One of skill in the art of spectral analysis is familiar with various methods of signal processing of the spectral output by curve fitting (see, for example, Winter, U.S. 4,791,577 (1988); Lodder, U.S. 5,124,932 (1992); and Stark, U.S. 5,379,238 (1995)). Further, the instant specification provides a detailed working example of how to generate a residual baseline (see page 18, lines 16-23 and Figures 23-25).

Thus, one of skill in the art, by virtue of applicant's teachings in the specification and known procedures in the art, would be able to generate a

Locating a probable peak

The Examiner contends that the step "locating a probable peak" is not enabled because the specification allegedly fails to recite the set of possible compositions or expected peaks, and urges that without knowing the expected peaks prior to the generation of the data, one of skill in the art allegedly would be unable to match putative peaks with the expected peaks and determine the probability that each putative peak in the data is an actual peak.

As a preliminary matter, Applicant respectfully submits that the Examiner states that the rejection is based on alleged lack of enablement of "locating a probable peak" while the argument made by the Examiner is directed to "determining the probability that each putative peak in the generated data is an actual peak." The examiner asserts that

> "one of skill in the art would be unable to match the putative peaks with the expected peaks thereby determining the probability of each putative peak in the generated data to be an actual peak indicative of the composition of the biological sample."

The Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. See *Ex parte* Sorenson, 3 USPQ2d 1462, 1463 (Bd. Pat. App. & Inter. 1987) (see, also MPEP 2163.04). In this instance, the Examiner has not provided any reasons why skilled persons would not recognize in the disclosure how to determine the location of expected peaks in a sample.

Irrespective of the Examiner failing to provide evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of steps for "locating a probable peak," Applicant respectfully asserts that the specification does provide guidance to one of skill in the art as

specification teaches locating probable peaks by matching putative peaks to the location of the expected peaks. The specification also teaches methods for

knowing the location of expected peaks. For example, on page 9, lines 15-19, the specification teaches in one embodiment that

> the biological sample is selected and processed to have only a limited range of possible compositions. Accordingly, it is therefore known where peaks indicating composition should be located, if present. Taking advantage of knowing the location of these expected peaks, in block 60 the method 35 matches putative peaks in the processed signal to the location of the expected peaks.

Thus, the specification teaches that by either selection or processing, the biological sample will have a limited range of possible compositions. Hence, there is no need to provide a set of all possible compositions of all possible biological samples in order to know the expected peaks in the biological sample being tested. Instead, the biological sample to be tested is either selected or processed so that it will have a limited range of possible compositions. Putative peaks in the processed signal are then matched to the location of the expected peaks to locate a probable peak (page 9, lines 17-19).

Thus, following the methods set forth in the specification, one of skill in the art can locate a probable peak in the corrected data set.

CONCLUSION

In light of the scope of the claims, the teachings in the specification, the high level of skill of those in this art, and the extensive knowledge of those of skill in this art, it would not require undue experimentation for a person of skill in the art to 1) apply a baseline correction to correct the baseline; 2) remove the residual baseline from the data set by application of techniques to smooth or curve fit the residual baseline, including application of a quartic polynomial fit; and 3) locate a probable peak using the location of expected peaks in a sample. Therefore, the specification is enabling for making and using the full scope of the claimed subject matter. Applicant respectfully requests that the rejection be

REJECTION OF CLAIMS 1-45 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH - SCOPE

Claims 1-45 are also rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the disclosed "generating a data set," "denoising the data set," "removing residual baseline effects," and "compressing the intermediate data set," allegedly does not reasonably provide enablement for any and all means, because the specification allegedly discloses no other embodiments to perform these steps. The Examiner states that the specification provides no working examples and no guidance on how any means other than those disclosed can be used to generate a data set, denoise the data set, remove residual baseline effects, and compress the intermediate data set, and thus argues that the disclosed steps are enabled but are not commensurate in scope with these claims. The Examiner concludes that one of skill in the art would not be able to practice the claimed invention without an undue amount of experimentation. This rejection is respectfully traversed.

RELEVANT LAW

The test of enablement is whether one skilled in the art can make and use what is claimed based upon the disclosure in the application and information known to those of skill in the art without undue experimentation. *United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). A certain amount of experimentation is permissible as long as it is not undue.

It is incumbent upon the examiner to first establish a *prima facie* case of non-enablement. *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369-70 (CCPA 1971). A patent application need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent , Inc.*, 3 USPQ2d 1737 (Fed. Cir. 1987). The requirements of 35 USC §112, first paragraph, can be fulfilled by the use of illustrative examples or by broad terminology. *In re*

> ...we do not regard section [illegible] first paragraph as requiring a specific example of everything within the scope of a broad claim ... What the Patent Office is here apparently attempting is to limit all

> claims to the specific examples, not withstanding the disclosure of a broader invention. This it may not do.

In re Grimme, Keil and Schmitz, 124 USPQ 449, 502 (CCPA 1960) :

> It is manifestly impracticable for an applicant who discloses a generic invention to give an example of every species falling within it, or even to name every such species. It is sufficient if the disclosure teaches those skilled in the art what the invention is and how to practice it.

This clause does not require "a specific example of everything *within the scope* of a broad claim." *In re Anderson*, 176 USPQ 331, at 333 (CCPA 1973), emphasis in original. Rather, the requirements of § 112, first paragraph "can be fulfilled by the use of illustrative examples **or** by broad terminology." *In re Marzocchi et al.*, 469 USPQ 367 (CCPA 1971)(emphasis added).

ANALYSIS

General techniques and conditions for generating a data set, denoising the data set, removing residual baseline effects, and compressing the data set are provided in the specification and are known to the skilled artisan, as discussed in detail below, and any necessary adjustment can be determined empirically using routine testing or even based on theoretical calculations. Having taught the requisite result to be achieved, it would not require undue experimentation to select appropriate conditions to achieve the desired result.

Generating a data set

The Examiner contends that the specification indicates that the generated "data is indicative of the mass of DNA fragments in the sample" (page 6, lines 10-25 and page 7, lines 1-20) and alleges that the specification fails to provide for any other means for generating a data set and none appear to have been known in the art.

The specification actually teaches that any test instrument that generates

(page 7, lines 6-13). One of skill in the art at the time of application would be

familiar with a number of instruments that generate a data set indicative of the components in a sample, and all of them can be used for testing biological samples. For example, such instruments include particle component analyzing apparatus (U.S. 5,319,966); optogalvanic spectrometers (U.S. 5,706,082); secondary ion mass spectrometers (U.S. 4,833,323); Raman spectrometers (U.S. 4,620,284); nuclear magnetic resonance (NMR) spectrometers, infrared spectrometers, mass spectrometers, ultraviolet spectrometers, and electron spin resonance spectrometers (Morrison *et al.*, *Organic Chemistry* (4th ed., 1983), pages 675-722); ion exchange chromatographs and gas chromatographs (Morrison *et al.*, page 1128); adsorption chromatographs (Robyt *et al.*, *Biochemical Techniques* (1987, pages 74-79); and gas-liquid chromatographs and high performance liquid chromatographs (Robyt *et al.*, pages 99-103).

Therefore, in light of the extensive teachings in the art and the knowledge of compositional analysis in the art, and the teachings of the specification, which include working examples, it would not require undue experimentation to generate a data set comprising data of the components in a biological sample as specified by the claims.

Denoising the data set

The Examiner alleges that denoising the data set is enabled only for the process of 1) performing a wavelet transformation to decompose the raw data into wavelet stage coefficients; 2) generating a noise profile from the highest stage of wavelet coefficients; and 3) applying a scaled profile to other stages in the wavelet transformation, and alleges that the specification fails to provide for other means for "denoising the data set" and that none appear to have been known in the art.

Applicant respectfully submits that many methods for "denoising" data [illegible] of skill in the art, and that wavelet transformation is but one [illegible] denoising data include digital filtering and finite impulse response (FIR) filtering (U.S. 5,885,841; 1999); fast Fourier transform and filters based on signal-to-

noise ratio (U.S. 6,032,114, February 2000); linear adaptive noise cancellation (U.S. 5,482,036; 1996); band pass filtering techniques (U.S. 4,955,379; 1990); logarithmic transformation and baseband filtering (5,924,980; 1999); peak subtraction methods using the Mann-Fenn algorithm (U.S. 5,072,115; 1991); and threshold filters and deconvolution equations (U.S. 5,635,713; 1997).

In addition, the specification provides for ways of "denoising the data set" other than wavelet transformation. The Examiner is directed to page 8, lines 5-6 of the specification, where the use of conventional Fourier analysis techniques to denoise the data is disclosed. Therefore, in light of the extensive teachings of denoising data in the art, and the teachings of the specification, which includes multiple examples of techniques to denoise data, it would not require undue experimentation for a skilled artisan to denoise the data set.

<u>**Defining putative peaks**</u>

The Examiner alleges that "defining putative peaks" is enabled only for the means where putative peak areas are systematically identified by taking a moving average along the signal and identifying sections of the signal which can exceed a threshold related to the moving average (citing page 14, lines 14-16 and page 17, lines 15-17), and alleges that no other means are provided and that none appear to have been known in the art, concluding that one of ordinary skill in the art would not have known how to practice the claimed subject matter.

The Applicant respectfully disagrees. The instant specification teaches that putative peaks are located in the data by setting a threshold below which peaks will be rejected, where the

> noise profile is used to generate a threshold which is applied to the data in each stage. Since the noise profile is already scaled to adjust for the noise content of each stage, calculating a threshold
>
> above the threshold are retained (page 12, lines 22-28)

The instant specification also teaches on page 14, lines 13-18 that:

> FIG. 13 shows that putative peak areas 145, 147, and 149 are located in the denoised and shifted signal 150. The putative peak areas are systematically identified by taking a moving average along the signal 150 and identifying sections of the signal 150 which exceed a threshold related to the moving average. It will be appreciated that **other methods can be used to identify putative peak areas** in the signal 150. (emphasis added)

Alternative methods are known in the art to define putative peaks by distinguishing them from inherent noise. For example, these include the use of spike rejection algorithms (U.S. 5,960,097, 1999); use of differential calculus operations of an even-numbered order (U.S. 5,745,369, 1998); use of principal component analysis, partial least squares techniques or taking the second derivative of the spectra using the Savitsky-Golay method (5,592,402, 1997).

Therefore, in light of the extensive teachings in the art and the knowledge of defining putative peaks in the art, and the teachings of the specification, it would not require undue experimentation for one of skill in the art to define putative peaks in the data set.

Removing residual baseline effects

The Examiner alleges that "removing residual baseline effects" is enabled only for the means where the center line of the putative peaks are identified and an area equal to twice the width of the Gaussian is removed from the left of the center line, while an area equivalent to 50 Daltons is removed from the right of the center line, citing page 18, lines 4-9 of the specification, and alleges that no other means are provided and that none appear to have been known in the art, concluding that one of ordinary skill in the art would not have known how to practice the claimed subject matter. Applicant respectfully disagrees.

The specification teaches on page 17, lines 27-30 that

> [illegible] are therefore removed to increase the accuracy and confidence in making identifications.

The instant specification teaches in one embodiment of removing residual baseline effects a method to remove residual baseline effects attributable to salt adducts (page 18, lines 6-15), where the

> peaks are removed by identifying a center line 230, 232, and 234 of the putative peaks 218, 222, and 224, respectively and removing an area both to the left and to the right of the identified center line. For each putative peak, an area equal to twice the width (W) of the Gaussian is removed from the left of the center line, while an area equivalent to 50 daltons is removed from the right of the center line. It has been found that the area representing 50 daltons is adequate to sufficiently remove the effect of salt adducts which may be associated with an actual peak. Such adducts appear to the right of an actual peak and are a natural effect from the chemistry involved in acquiring a mass spectrum. Although a 50 Dalton buffer has been selected, it will be appreciated that **other ranges or methods can be used to reduce or eliminate adduct effects.** (emphasis added)

Alternative methods are known in the art to remove residual baseline effects. For example, Brown *et al.* teaches methods for correcting spectral data to remove data due to the measurement process itself, such as spectral baseline variations, the methods including modelling variation in the baseline by a set of orthogonal, frequency-dependent polynomials and singular value decomposition to generate a computer simulation of the background, use of Legendre polynomials, Gram-Schmidt orthogonalization, and the constrained principal spectral analysis algorithm (U.S. 5,121,337; 1992). Abramovitch *et al.* teaches methods of removing residual baseline effects by using statistical two-way analysis of variance on demodulated signal (ANOVA) or the Pareto decoupling method (U.S. 5,909,661; 1999). O'Rourke *et al.* teaches removing residual baseline effects by computing the second derivative of the average spectrum (U.S. 5,131,746; 1992). Further, Monforte *et al.* teaches that salt adducts can

Therefore, in light of the extensive teachings in the art and the knowledge of removing residual baseline effects in the art, and the teachings of the specification, it would not require undue experimentation for one of skill in the art to remove residual baseline effects in the data set.

__Compressing the intermediate data set__

The Examiner alleges that "compressing the intermediate data set" is enabled only for the means taught on page 16, lines 5-8, where the first point of the intermediate data file becomes the starting point for the compressed data, and thereafter each data point is calculated by replacing the whole number portion (left of the decimal) with the difference between the current and the last whole number, while the remainder (right of the decimal) remains intact. The Examiner alleges that no other means are provided and that none appear to have been known in the art, concluding that one of ordinary skill in the art would not have known how to practice the claimed subject matter.

It is respectfully submitted that data compression is well known in the art, as evidenced by the extensive teachings in the art regarding data compression. For example, in U.S. Patent 5,995,989 "*Method and apparatus for compression and filtering of data associated with spectrometry*", Gedcke *et al.* teaches a method for compressing spectrometry data, and further teaches that other compression methods are known to those of skill in the art (column 1, line 39 through column 2, line 12):

> In U.S. Pat. No. 5,592,402, Beebe *et al.* teach a method for comparing spectra typically acquired from a chromatograph run on a production sample to the spectral features from a calibration standard for the purpose of detecting a maverick spectrum or for detecting a sample whose composition lies outside tolerable limits. Beebe *et al.* describes methods for separating a spectrum into components comprising peaks, background, and noise. These methods are well-known in the art as described by Coldwell, Robert [illegible] Jenkins, Ron, R. W. Gould, and Dale Gedcke, Quantitative X-Ray Spectrometry, Chapter 6, Marcel Dekker, New York, 1981; Bevington, Phillip R., and D. Keith Robinson, Data Reduction and

Error Analysis for the Physical Sciences, McGraw-Hill, New York, 1969; and Mariscotti, M. A., Nucl. Instrum. & Methods, 50, page 309 (1967).

U.S. Pat. No. 5,428,357 issued to D. Haab *et al.*, discloses a method for compressing data to achieve high speed data acquisition. The data compression schemes disclosed by Haab *et al.* involve generating a first difference spectrum and coding sequentially repeated numbers by the common value and a number that specifies the number of times that number is repeated. However, Haab *et al.* do not disclose a method for determining which portions of the data are not useful and which, therefore, may be discarded. Accordingly, unwanted data, though potentially compressed, is maintained.

U.S. Pat. No. 4,490,806 issued to C. G. Enke *et al.*, teaches yet another method for data compression associated with spectral analysis. In the method disclosed by Enke *et al.*, a fixed threshold is assigned to the data, with any data above the threshold being kept as peak data and any data below the threshold being discarded as background noise.

In addition, alternate data compression methods are known in the art, and these include wavelet compression (U. S. 6,094,050); compression using look-up tables (U.S. 5,981,946); logarithmic differential compression (U.S. 5,933,360); index mapping techniques, scalar quantization and vector quantization (U.S. 5,910,853); use of a two dimensional concatenated matrix (U.S. 5,490,516); and use of a truncated Fourier series (U.S. 5,498,875, 1996).

Therefore, in light of the extensive teachings in the art and the knowledge of data compression in the art, and the teachings of the specification, it would not require undue experimentation for one of skill in the art to compress the intermediate data set.

Entitlement to broader claims than only the disclosed conditions

The Office Action alleges that the claims are enabled only for what applicant has specifically exemplified. Applicant respectfully submits that all

[illegible] and residual baseline effects" and "[illegible]ompressing the intermediate data set" known to one of skill in the art are contemplated to be within the scope of

claims. The specification discloses exemplary embodiments of each. Numerous alternate embodiments are known to those of skill in the art, as evidenced by the references made of record and discussed above.

A patentee not only is entitled to narrow claims particularly directed to the preferred embodiment, but also to broad claims that define the invention without a reference to specific instrumentalities. *Smith v. Snow*, 294 U.S. 1, 11, 24 USPQ 26, 30 (1935). The requirements of 35 USC §112, first paragraph, can be fulfilled by the use of illustrative examples or by broad terminology, and the Patent Office may not limit all claims to the specific examples. *In re Anderson*, 176 USPQ 331, 333 (CCPA 1973). Applicant is entitled to claims that are commensurate in scope not only with what applicant has specifically exemplified, but commensurate in scope with that which one of skill in the art could obtain by virtue of that which the applicant has disclosed.

The specification recites that the instant discovery involves the steps of "generating a data set," "denoising the data set," "removing residual baseline effects" and "compressing the intermediate data set." The only reasoning the Examiner provides as to why the specific examples of "generating a data set," "denoising the data set," "removing residual baseline effects" or "compressing the intermediate data set" exemplified in the specification and coupled with the disclosure in the application are allegedly not enabling with respect to the claims is that the specification allegedly fails to provide other ways for "generating a data set," "denoising the data set," "removing residual baseline effects" or "compressing the intermediate data set" and contends that none are known in the art. Applicant notes that the Examiner states that the exemplified steps **are enabled** in the specification (paper number 13, page 5). The mere fact that the precise steps of the embodiment exemplified in the specification are not recited in the claims does not provide sufficient reason to hold the claims non-enabled

[illegible]

laims recite specific steps for "generating a data set," "denoising the data set" "removing residual baseline effects" or "compressing the intermediate data set"

or even that the specification recite specific steps for all circumstances, when such steps can be readily determined by one skilled in the art. As discussed in detail above, various methods for "generating a data set," "denoising the data set," "removing residual baseline effects" or "compressing the intermediate data set" are known in the art. Reciting precise steps in the claims would be unduly limiting and should not be required.

In this instance, applicant is providing a general method for identifying a biological sample by analyzing information received from a test instrument. To limit the claims to specific steps for "generating a data set," "denoising the data set," "removing residual baseline effects" or "compressing the intermediate data set" would permit those of skill in the art to practice the claimed system and method, but avoid infringement, merely by substituting different steps to achieve the same outcome, which could be readily identified using the methods described in the specification and known in the art. Further, it is contrary to the public policy and constitutional mandate that underlie the U.S. patent system and upon which the U.S. patent laws are based to require Applicant to limit the claims to only the specifically exemplified embodiments.

> "The public purpose on which the patent law rests requires the granting of claims commensurate in scope with the invention disclosed. This requires as much the granting of broad claims on broad inventions as it does the granting of more specific claims on more specific inventions" *In re Sus and Schafer*, 49 CCPA 1301, 306 F.2d 494, 134 USPQ 301, at 304.

Therefore, in light of the scope of the claims, which are tailored to the scope of the disclosure, the extensive description in the application and the high level of skill of those in this art, it would not require undue experimentation to practice the systems and methods as claimed. It is respectfully submitted that the rejections of claims 1-45 under 35 U.S.C. § 112, first paragraph, are

REJECTION OF CLAIMS 1-45 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-45 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly being vague and indefinite because the recitations "compositional data," "composition," "component" and "responsive" fail to particularly point out the limitations to which the recitations refer in the methods and systems.

This rejection is respectfully traversed.

RELEVANT LAW

Claims are not read in a vacuum but instead are considered in light of the specification and the general understanding of the skilled artisan. Rosemount Inc. v. Beckman Instruments, Inc., 727 F.2d 1540, 1547, 221 USPQ 1, 7 (Fed. Cir. 1984), Caterpillar Tractor Co. v. Berco, S.P.A., 714 F.2d 1110, 1116, 219 USPQ 185, 188 (Fed. Cir. 1983). A claim is not indefinite when one skilled in the art would understand the language in the claims when read in light of the specification.

35 U.S.C. § 112, second paragraph requires only reasonable precision in delineating the bounds of the claimed invention. Claim language is satisfactory if it reasonably apprises those of skill in the art of the bounds of the claimed invention and is as precise as the subject matter permits. Shatterproof Glass Corp. v. Libby-Owens Ford Col., 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir.), cert. dismissed, 106 S.Ct. 340 (1985).

During patent examination, the pending claims must be given the broadest reasonable interpretation consistent with the specification. *In re Morris*, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed.Cir. 1997). The words of a claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz, 893, F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed.Cir. 1989). The claims are definite if they "make clear what subject matter they encompass and thus what the patent precludes

ANALYSIS

"Compositional data" and "Composition"

The Examiner alleges that the use of the recitations "compositional data" and "composition" in claims 1, 38, 40 and 41 and their dependent claims is vague and indefinite, and suggests that the issue can be resolved by particularly pointing out the limitations of "compositional data" and "composition" as utilized in the method.

Applicant respectfully submits that amendment of claims 1, 38, 40 and 41 herein obviates this objection. Applicant respectfully requests that the rejection be withdrawn.

"Component"

The Examiner alleges that the use of the recitation "component" in line 4 of claim 45 is vague and indefinite. Applicant respectfully submits that the term "component" is a term understood by artisans in diverse disciplines, and is so wide-spread in use that it is used in the ordinary American vernacular, as evidenced by its appearance in collegiate dictionaries. Applicant directs the Examiner's attention to *Webster's II New College Dictionary*, (1995), page 230, which teaches that a component, when referring to the chemical discipline, refers to any of the minimum number of substances required to specify completely the composition of all phases of a chemical system (meaning 4). Further, *Stedman's Medical Dictionary* (26th ed., 1995) defines "component" on page 375 as "an element forming a part of the whole." Thus the plain meaning of the word "component" would be known to one of skill in the art, and reasonably apprises those of skill in the art of the bounds of the claimed invention.

Applicant respectfully requests that the rejection be reconsidered and

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AMENDMENT

"Responsive"

The Examiner alleges that the use of the recitation "responsive to the calculated probability" in line 16 of claim 45 is vague and indefinite. Applicant respectfully submits that amendment of claim 45 herein obviates this objection.

Applicant respectfully requests that the rejection be withdrawn.

* * *

In view of the remarks herein, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
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MAY 2 1 2003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Yip

Serial No.: 09/663,968
Customer No.: 24961
Confirmation No.: 4499

Filed: September 19, 2000

For: *METHOD AND DEVICE FOR IDENTIFYING BIOLOGICAL SAMPLES*

Art Unit: 1631

Examiner: Mahatan, C.

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Michael Lough

ATTACHMENT TO THE AMENDMENT SHOWING MARKED UP PARAGRAPHS AND CLAIMS (37 CFR §1.121)

Please amend claims 1 as follows (insertions are underlined, deletions are [bracketed]:

1. (3x Amended) A method for identifying a biological sample, comprising:

generating a data set comprising [compositional] data of the components in [regarding] the biological sample;

denoising the data set to generate denoised data;

correcting the baseline from the denoised data to generate an intermediate data set;

defining putative peaks for the biological sample;

using the putative peaks to remove residual baseline effects, generating a residual baseline;

removing the residual baseline from the intermediate data set to generate a corrected data set;

locating a probable peak in the corrected data set; and

identifying, using the located probable peak, the biological sample.

system comprising:

an instrument receiving the biological sample and generating a data set

comprising data [indicative] of the [composition of] components in the biological sample;

a computer communicating to the instrument and configured to receive the generated data set, the computer performing the method of:

denoising the data set to generate denoised data;

correcting the baseline from the denoised data to generate an intermediate data set;

defining putative peaks for the biological sample;

using the putative peaks to remove residual baseline effects, generating a residual baseline;

removing the residual baseline from the intermediate data set to generate a corrected data set;

locating a probable peak in the corrected data set; and

identifying, using the located probable peak, the biological sample.

40. (2x Amended) A machine readable program operating on a computing device, the computing device being configured to receive a data set comprising data of the [indicating composition of] components in a biological sample, wherein the program implements [implement] the steps of:

denoising the data set to generate denoised data;

correcting the baseline from the denoised data to generate an intermediate data set;

defining putative peaks for the biological sample;

using the putative peaks to remove residual baseline effects, generating a residual baseline;

removing the residual baseline from the intermediate data set to generate a corrected data set;

[illegible]

identifying, using the located probable peak, the biological sample.

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Yip
MARKED-UP CLAIMS

41. (2x Amended) A system for identifying a component of a DNA sample, comprising:

a mass spectrometer receiving the DNA sample and generating a data set comprising data [indicative] of the [composition of] components in the DNA sample;

a computing device configured to receive the data set, the computing device implementing the method comprising:

denoising the data set to generate denoised data;

correcting the baseline from the denoised data to generate a corrected data set, the corrected data set having putative peaks;

using the putative peaks to remove residual baseline effects;

locating a probable peak in the corrected data set; and

identifying, using the located probable peak, a component in the composition of the DNA sample.

45. (2x Amended) A system for identifying a component in a biological sample, comprising:

an instrument receiving the biological sample and generating a data set comprising data [indicative] of the components [component] in the biological sample;

a computing device receiving the data set and performing the steps of:

generating corrected data by processing the data set to remove noise due to system and chemical reaction characteristics, the corrected data set having putative peak areas;

using the putative peaks to remove residual baseline effects;

defining the position of expected peaks using known possible peak areas from the biological sample;

[illegible] expected peaks

calculating a [the] probability that the putative peaks in the shifted

data set are actual peaks;

determining a confidence of the probability; and

if the confidence exceeds a threshold value, [calling the composition of the biological sample responsive to the calculated probability] using the putative peaks to [thereby] identify a component in the sample.

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Michael Lough

SUPPORTING DOCUMENTS

1. Morrison *et al.*, *Organic Chemistry* (4th ed., 1983), pages 675-722 and 1128.

2. Robyt *et al.*, *Biochemical Techniques - Theory and Practice* (1987), pages 73-79 and 99-103.

3. Stedman's Medical Dictionary (26th ed., Williams & Wilkins, 1995), page 375.

4. Webster's II New College Dictionary (1995), page 230.